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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,188	12/21/2001	Charles S. Zuker	02307E-114910US	9521

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EXAMINER

BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
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1649

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/026,188

Applicant(s)

ZUKER ET AL.

Examiner

Michael Brannock

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 12-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 12-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Application: Claims and Amendments

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Applicant is notified that the amendments put forth on May 5, 2005 have been entered in full.

Response to Amendment

The Objection to the Oath/Declaration is withdrawn as the inventors addresses are provided on the Application Data Sheet.

The objection to the specification is withdrawn in view of Applicant's amendments.

Applicant is reminded that the claims will be examined only to the extent that they read on the elected SEQ ID NO: 8.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 12-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require either methods of identifying a compound that modulates taste signaling (claim 1) or methods of modulating taste signaling. The words "modulates" and "modulating" in the claims render the claims indefinite because the words are indefinite terms and neither the claim nor the specification sets forth what physical processes are intended to be encompassed in the scope of the term and what are not, thus the metes and bounds of the claim cannot be determined. At page 11, last paragraph, of the specification the word "modulates" is distinguished from the words "inhibitors" and "activators" yet no definition is provided that sets forth what properties distinguishes a modulator from an activator or inhibitor. Thus the artisan could not understand the meaning of the term and could therefore not be able to determine the metes and bounds of the claim.

Similarly, the phrase "functional effect" in the claims renders the claims indefinite because the term is indefinite and neither the claim nor the specification sets forth what physical processes are intended to be encompassed in the scope of the term and what are not, thus the metes and bounds of the claim cannot be determined. At page 11 of the specification the term is defined as follows:

"Determining the functional effect" denotes assays for a compound that increases or decreases a parameter that is indirectly or directly under the influence of TC-ICS. Such functional effects are measured by any means known to those skilled in the art, e.g., patch clamping, voltage-sensitive dyes, whole cell currents, radioisotope efflux, inducible markers, oocyte or tissue culture cell expression of TC-ICS; transcriptional activation of TC-ICS; ligand binding assays', voltage, membrane potential and conductance changes; ion flux assays', changes in intracellular second messengers such as

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cA'Mp and inositol triphosphate (IP3); changes in intracellular calcium levels; neurotransmitter release, and the like.

The phrase "under the influence of TC-ICS" in this definition remains undefined and the rest of the definition is only by way examples that do not set forth metes and bounds of the claims.

Thus, an artisan would not know what properties would be considered to be under the influence of TC-ICS, and thus could not reasonably determine the metes and bounds of the claim.

Claim 1 required the step of forming a functional ion channel yet the specification has not set forth what procedure for determining whether or not the polypeptide of SEQ ID NO: 8 is functional or not. Thus, the artisan could not know whether or not he or she was practicing the claimed invention.

The claim 1(ii) requires the step of determining a functional effect of the compound on a predetermined ion. The word "predetermined" renders the claim indefinite because the claim does not set forth what parameters what constitute predetermination. One skilled in the art could not know if he were infringing on Applicant's claims because he could not be sure if the ion was predetermined. It is suggest to Applicant that this word is not necessary in the claim and might ultimately unnecessarily limit the scope.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification proposes that at least one of SEQ ID NO: 2, 5, and 8 are taste receptors that modulate taste perception. Also proposed are a multitude of assays, used in the art to study particular biochemical pathways involved with different aspects taste signal transduction as well as signal transduction in general; see pages 23-28. Yet in order to practice the invention as claimed, one skilled in the art would need to know which of these assays and which materials, could be used in conjunction with the polypeptide of SEQ ID NO: 8. The specification admits that it is well recognized in the art that the signal transduction schemes underlying taste transduction are bewilderingly complex and poorly understood, page 3. Thus, at best, at the time of filing one of skill in the art would expect that to carry out an extensive research plan to try to use the invention as claimed, if that can be done, would be unduly burdensome.

Furthermore, claim 1(ii) requires the step of determining a functional effect of the compound upon a transmembrane ion flux of a predetermined ion. Thus, the claim requires a method of selecting the ion before the step of determining the functional effect, yet the

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specification has not put forth what parameters are required of the this selection method.

Therefore an artisan would not know how to practice the claimed invention.

Additionally, claims have been amended to require the step of forming a functional ion channel, yet the specification has not disclosed what steps to follow to determine if a functional channel has been formed. The specification does not teach what ligand would open the channel so that one could measure the ion flux so as to know that it is functional.

Furthermore, claims 12-15 encompass, but do not require, compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8. There is no teaching of compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8 and one of skill in the art would view the invitation to randomly sample chemicals in the hope of finding such would be unduly burdensome.

Additionally, the claims are directed to the use of amino acid sequence variants of SEQ ID NO: 8; *should* Applicant establish that the specification is enabling for assays to measure modulation of taste signaling as claimed with regard to SEQ ID NO: 8, the specification has failed to teach which amino acid substitutions should be made in SEQ ID NO: 8 so as to preserve any function of SEQ ID NO: 8, as discussed above.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or

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regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 8 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Due to the large quantity of experimentation necessary to generate the infinite number of variants required by the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of specific teachings as to which signal transduction pathways should be

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monitored, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Applicant argues (last line of page 9) that changes in parameters upstream from the associated proteins [i.e. transduction proteins] can still be used. For example, changed ion flux mediated by the ion channel can be such an upstream event.

This argument is persuasive, as this was essentially done by Lui-D et al. using the excised patch pipette technique. SEQ ID NO: 8 was found to be a non-selective monvalent cation channel gated by Ca^{++} , see Abstract and of Liu-D et al., PNAS 100(25)15160-15165, 2003. However the claims are not limited to this technique, and the issues involving “forming a function ion channel” and determining a functional effect on “a predetermined ion” remain. Additionally, it should be pointed out that Lui-D et al. obtained whole cell recordings only with coexpression of the muscarinic M1 receptor or application of a Ca^{++} ionophore, see pages 15163-15164.

Applicant argues that one of skill in the art would know how to identify and to create amino acid substitution variants of SEQ ID NO: 8, e.g. polymorphic alleles and man made mutants, and that it is routine in the art to make mutations in a polypeptide and to test these variants. This argument has been fully considered but not deemed persuasive because the specification has not taught what these muteins would be tested for. The issue is not that sequence variants could be created, but that the specification has not taught which variants, of

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the almost infinite number of variants that could be created, could be made that preserve and/or create any desired functional property of the polypeptide. Nor has the specification taught how to use any of the claimed polynucleotides that encode variants but which do not have any asserted functional properties. While it may be true that functional variants typically contain only conservative variation or variation in non-critical residues or non-critical regions, this teaching does not provide any information as to where these sites of conservative variation, non-critical residues, or non-critical regions could be - such information being necessary to enable the skilled artisan to make and use the claimed invention without undue experimentation. Further, the specification failed to provide guidance as to what any particular functional property of the claimed polypeptide is; nor any particular functional difference between the polypeptide and sequence variants of the polypeptide. Thus, one of skill in the art would not know how to create a variant of a polypeptide having a particular function if that function was not known nor if there were no teachings as to how to produce that function, e.g. agonist binding, so as to test the variants for functionality.

Claims 1-9 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification proposes that at least on of SEQ ID NO: 2, 5, and 8 are taste receptors that modulate taste perception. Also proposed are a multitude of assays, used in the art to study particular biochemical pathways involved with different aspects taste signal transduction as well

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as signal transduction in general, see pages 23-28. Yet in order to practice the invention as claimed, one skilled in the art would need to know which of these assays and which materials, could be used in conjunction with the polypeptide of SEQ ID NO: 8. The specification admits that it is well recognized in the art that the signal transduction schemes underlying taste transduction are bewilderingly complex and poorly understood, page 3. Never-the-less claims 1-9 are directed to broad assay methods that cover practically every conceivable means of studying intracellular signal transduction whereas one skilled in the art would recognize that only the patch pipette technique could be used given the limited teachings in the specification and the general knowledge in the art, and thus Applicant does not appear to be in possession of the scope of these claims.

Additionally, claims have been amended to require the step of forming a functional ion channel, yet the specification has not disclosed what steps to follow to determine if a functional channel has been formed. The specification does not teach what ligand would open the channel so that one could measure the ion flux so as to know that it is functional. There is no evidence in the specification that demonstrates that Applicant either produced a functional ion channel or know how to produce a functional ion channel with SEQ ID NO: 8. Thus one skilled in the art would not view that Applicant was in possession of the claimed invention.

Furthermore, claims 12-15 encompass, but do not require, compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8. There is no teaching of compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8, thus there is no evidence Applicant was in possession of such. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's

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were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Additionally, the specification discloses the polypeptide of SEQ ID NO: 8 yet the claims encompass assays involving an essentially limitless genus of polypeptides not described in the specification, i.e. polynucleotides sequences from other species, mutated sequences, allelic variants, and sequences that need only 90% identity with SEQ ID NO: 8. yet which retain the required functional limitations. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist or could exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of three polynucleotides does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, only one sequence at least 90% identical to SEQ ID NO: 8, which is SEQ ID NO: 8 itself, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

With the exception of polynucleotides encoding polypeptides of SEQ ID NO: 8 referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only the polypeptide of SEQ ID NO: 8, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant argues that other TRP were known in the art and that polypeptides representative of the genus could readily be produced and verified. This argument has been fully considered but not deemed persuasive, for the reasons stated above. Additionally, it should be pointed out that SEQ ID NO: 2 and 5 do not appear to be encompassed by the genus of polypeptides 90% identical to SEQ ID NO: 8 and therefore could not be representative of it.

Applicant's arguments regarding Fiddes are persuasive in part, except that the principle is that Applicant is claiming an assay of a large genus of polypeptides wherein no specific information as to the identity of any particular member, except one, is given.

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Applicant argues that Lilly did not require the possession of every embodiment of the species. This argument has been fully considered but not deemed persuasive as this principle was not the basis of the rejection.

Applicant argues that the specification teaches methods for verifying the function of an ion channel. This argument has been fully considered but not deemed persuasive. One skilled in the art would view the broad teachings of pages 23-28 as simply a survey of general methods of studying signal transduction and not as specific instructions to be used to verify the functionality of a polypeptide of SEQ ID NO: 8, e.g. no ligand or activator of the polypeptide is taught. Thus, one could not know whether the channel was functional unless a ligand is discovered.

Applicant argues that the structural features of members of the genus have been described in detail. This argument has been fully considered but not deemed persuasive. One skilled in the art appreciates that the recitation of percent identity to SEQ ID NO: 8 describes no structure other than SEQ ID NO: 8. Percent identity describes no particular amino acid sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 1-6, 8, 12, 14 stand rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Publication 2002/0037515, published March 28, 2002, which is fully supported by prior provisional application, US 60/197,491, filed April 17, 2000, as set forth previously and reiterated below.

US Patent Publication 2002/0037515 discloses a polypeptide TRP8 that is identical to the instant SEQ ID NO: 8 with the two exceptions that the glutamine at position 630 is missing in TRP8 and threonine is substituted for Aspartic acid at position 990. Never-the-less, TRP8 is asserted to be a taste-cell receptor protein that modulates taste transduction, see the Abstract. The production of Antibodies is disclosed (paragraph 0049) and taught to be used in screening assays to identify modulators of taste transduction see section 5.5. Further, US Patent Publication 2002/0037515 discloses a particular voltage clamp assay that measures the effect of modulators on Calcium mediated activation of the TRP8, see section 6.2.5.

Methods of using these identified modulators to modulate taste signaling in humans are also contemplated, e.g. paragraph 10.

Applicant argues that the 1.131 Declaration (Drs. Zuker and Zhang) asserts that the claimed invention was completed before the filing date of US 60/197,491, filed April 17, 2000. This argument has been fully considered but not deemed persuasive. 37 CFR1.131(a)1 requires that the oath or declaration must include facts showing a completion of the invention. It appears that the Declaration simply asserts possession of a clone (clone 501) before April 17, 2000. This clone is asserted to be one of three that make up contig No. 068-3 157 501, and this contig is listed as being 629 base pairs in length. The instant SEQ ID NO: 8 consists of 1165 amino acids, and thus the minimum length required to encode it is 3495 base pairs. Contig No. 068-3 157 501

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is less than 20% of this required length. Thus the Declaration does not establish that applicant completed the claim invention prior to April 17, 2000.

Claims 12-15 rejected under 35 U.S.C. 102(b) as being anticipated by Madden-AM et al., Hepatology 26(1)40-48, 1997. Claims 12-15 require administration, to an individual, of a compound that modulates taste.. The claims require that the compound modulates taste signaling by an ion channel having a sequence identity greater than about 90% to SEQ ID NO: 8. The claims do not require that the individual has such an ion channel, only that the compound is capable of modulating it. Furthermore, the claims do not require that the compound directly modulates the ion channel. These claims read on the act of eating. Madden-AM et al. teach administration of bitter, salt, sweet and sour compounds to human subjects, which, absent evidence to the contrary would modulate, indirectly, the ion channel of SEQ ID NO: 8.

Claims 1-4 are rejected under 35 U.S.C. 102(anticipated) as being anticipated by the Abstract of Bernhardt-SJ et al., J. Physiol. 490(325-336)1996, who disclose a method of identifying a compound (e.g. sucrose) that modulates taste signaling in taste cells comprising contacting the compound with a eukaryotic host cell (rat circumvallate cells) which would be expected to express a polypeptide at 90% identical to the instant SEQ ID NO: 2 (which is disclosed as being from a rat) and would form a functional channel absent evidence to the contrary, and determining a functional effect (changes in intracellular calcium concentration) using ion sensitive dyes (e.g. Ca^{2+} imaging). It is noted that the claims do not require that the transmembrane ion flux be that of either SEQ ID NO: 2, 5, 8, rather this influx could be the Ca^{2+}

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influx into the cytoplasm from intracellular stores - which is what is detected by Bernhardt-SJ et al.

Claims 1, 2, 4-7 are rejected under 35 U.S.C. 102(anticipated) as being anticipated by Doolin-RE et al., J. Gen Physiol 107(545-554)1996 who disclose a method of identifying a compound (e.g. amiloride, see Fig 4) that modulates taste signaling in taste cells comprising contacting the compound with a eukaryotic host cell (rat circumvallate cells, see fig 4) which would express a polypeptide at 90% identical to the instant SEQ ID NO: 2 (which is disclosed as being from a rat) and would form a functional channel absent evidence to the contrary, and determining a functional effect either as changes in intracellular ion concentration and ion flux (whole-cell recording), and where the membrane is attached to a solid support e.g. pipette (patch pipette technique), page 547.

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Conclusion

Please note the new central fax number for official correspondence below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

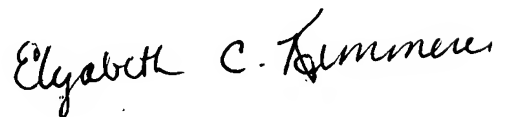
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB



July 22, 2005



**ELIZABETH KEMMERER
PRIMARY EXAMINER**